GE Healthcare
www.ge.com

Tackling cancer immunotherapy clinical trial challenges with personalized diagnostics

GE Healthcare is developing radiopharmaceuticals that can match the most appropriate treatment to a patient, which will help physicians initiate a beneficial treatment regime and could reduce the time that a patient receives an ineffective therapy.

Immunotherapies have transformed cancer care in recent years, significantly improving health outcomes in a range of hard-to-treat diseases. Developers of immunotherapies, however, face a challenge because only 20% to 40% of patients respond to checkpoint inhibitors, the main class of currently approved cancer immunotherapy.

Checkpoint inhibitors can have deep, durable effects, but they are ineffective in more than half of patients. Identifying the right patient for the right therapy can avoid administering costly treatment regimes with potential adverse side effects, and help to ensure timely delivery of the most effective treatments.

Another challenge relates to how researchers determine whether a patient is responding to therapy. Response evaluation criteria in solid tumors (RECIST) is the standard approach, but, depending on the tumor type, it can take months to deliver a result. The lag between the initiation of treatment and the determination of whether a patient is responding prevents physicians from quickly switching non-responders to alternative treatment pathways.

Building a suite of solutions

GE Healthcare's Pharmaceutical Diagnostics business is developing an ^{18}F-CD8 positron emission tomography (PET) imaging radiopharmaceutical to address both challenges. Diagnostic radiopharmaceuticals are currently used to image tumor-specific targets. There is a growing trend to use radiopharmaceuticals to image immune system biomarkers. The new wave of radiopharmaceuticals may increase immunotherapy treatment effectiveness by enabling study sponsors to identify patients with 'hot' tumors that are most likely to respond to immune checkpoint inhibitors. Equipped with these insights, sponsors can limit enrolment to patients with high tumor infiltration of CD8$^+$ T cells.

Additionally, after treatment such radiopharmaceuticals could provide an early signal of whole-body responses by establishing whether an immunotherapy has made a 'cold' tumor 'hot'. Rather than waiting months for RECIST, physicians can potentially use these tools within the first week or two to indicate whether a patient has elicited the level of immune response needed to shrink or eliminate a tumor.

Both uses of the radiopharmaceutical could reduce the time patients spend on ineffective therapies, first by avoiding unnecessary dosing of people who are unlikely to respond and then by enabling physicians to switch non-responders to alternative medications sooner.

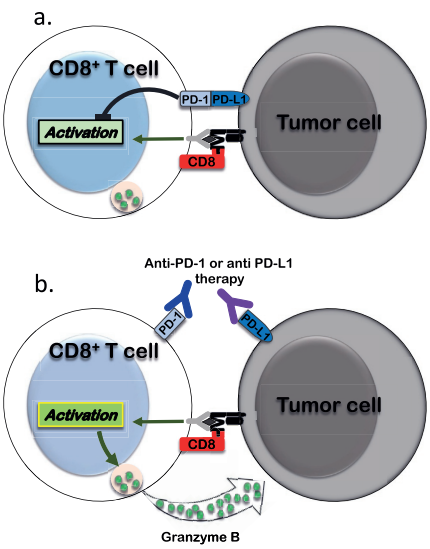

Fig. 1 | T cell interactions. Schematics explaining T cell interactions when non-activated (a) and activated. The tracer targets the enzyme Granzyme B, which is released when cytotoxic CD8$^+$ T cells are activated, and shows whether the immune system is attacking the tumor (b).

For drug developers, those benefits could increase clinical trial success rates by targeting investigational drugs to patients who are most likely to respond, therefore reducing the number of patients needed, the costs and the time of development. In summary, enriching clinical development would facilitate timely access to effective therapies, therefore improving the impact on patient lives.

If approved, in future the benefits could reach beyond clinical trials and enable the right therapies to be administered to the right patients in clinical practice, bringing economic as well as health benefits.

The ^{18}F-CD8 PET imaging radiopharmaceutical is positioned to become an important clinical trial tool for immunotherapy developers, but no single product can address all the unmet needs. Recognizing that, GE Healthcare is developing additional tools, including its Granzyme B PET tracer.

The tracer targets Granzyme B, an enzyme that is released when cytotoxic CD8$^+$ T cells are activated, and in doing so shows whether the immune system is attacking the tumor (Fig. 1). Like the ^{18}F-CD8 PET radiopharmaceutical, the Granzyme B PET tracer could provide early insights into whether a patient is responding to therapy, in this case by providing information on T cell activation and whole-body anti-tumor activity.

GE Healthcare's pursuit of solutions to today's immunotherapy challenges goes beyond PET imaging. The company is also developing artificial intelligence models designed to improve the identification of people who are more likely to respond to immunotherapy or experience adverse events.

Partnering to enhance immunotherapy trials

The progress of the suite of solutions points to the future of GE Healthcare's Pharmaceutical Diagnostics unit, a global leader in imaging agents used to support around 100 million procedures per year globally, and sets the stage for immunotherapy partnerships. By partnering, biopharma companies can enrich and enhance clinical trials and develop a new class of complementary and companion imaging diagnostics to individualize diagnosis and treatment planning.

"We want to help immunotherapy developers determine the optimal patient profile for a particular treatment pathway both in clinical trials and, ultimately, in clinical practice," said Usankar Thiru, Global Business Unit Leader, Immuno-Oncology at GE Healthcare. "Sponsors who share that focus and want to solve their immunotherapy clinical trial challenges should contact our team to discuss partnering opportunities. Through such partnerships, we can advance our shared goal of unlocking the potential of immunotherapies and delivering life-changing treatments to cancer patients."

CONTACT
Usankar Thiru, Global Business Unit Leader, Immuno-Oncology
GE Healthcare
Chalfont St Giles, UK
Tel: +44 1494 544000
Email: immuno.diagnostics@ge.com